

In re Application of:  
Jean-Pierre Issa  
Application No.: 09/398,522  
Filed: September 15, 1999  
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Attorney Docket No.: JHU1590

**In the Claims**

Please cancel claims 1-9, 16-18, 20, 24-32, and 34-36, without prejudice.

Please amend the claims as follows:

Claims 1-9 (Cancel)

Claims 11-15 (Previously canceled)

10. (Currently amended) A method for detecting colorectal adenoma or a cancer other than glioma, ~~associated with APOB, CACNA1G, CDX2, EGFR, FBN1, GPR37, HSPA6, IQGAP2, KL, PAR2, PITX2, PTCH, SDC1 or SDC4~~ comprising:

- a) contacting a nucleic acid-containing specimen from a subject with an agent that provides a determination of the methylation state of at least one of a first region and a second region of a CpG island of a gene or associated regulatory region of the gene;

~~wherein the gene is selected from the group consisting of APOB,~~

CACNA1G, wherein the first region is a region of the CACNA1G CpG island that is amplified by SEQ ID NO:33 and

SEQ ID NO:34, and wherein the second region is a region of the

CACNA1G CpG island that is amplified by SEQ ID NO:35 and

SEQ ID NO:36, CDX2, EGFR, FBN1, GPR37, HSPA6, IQGAP2,

KL, PAR2, PITX2, PTCH, SDC1, SDC4 and combinations thereof

and

- b) detecting hypermethylation of at least one of the first region and the second region a region of the gene or regulatory region, wherein hypermethylation of a at least one of the first region and the second region as compared to the same region of the CACNA1G gene or associated regulatory region in a subject not having said cancer

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colorectal adenoma or a cancer other than glioma is indicative of the colorectal adenoma or cancer other than glioma.

Claims 16-18 (Cancel)

19. (Currently amended) The method of claim 10, wherein the agent is a pair of primers that amplify the first region or the second region ~~hybridize with a target sequence in the gene or associated regulatory region of the gene.~~

20. (Cancel)

21. (Currently amended) The method of claim ~~20~~ 19, wherein the primer pair is ~~selected from the group consisting of SEQ ID NO:1 and 2, SEQ ID NO:3 and 4, SEQ ID NO:5 and 6, SEQ ID NO:7 and 8, SEQ ID NO:9 and 10, SEQ ID NO:11 and 12, SEQ ID NO:13 and 14, SEQ ID NO:15 and 16, SEQ ID NO:17 and 18, SEQ ID NO:19 and 20, SEQ ID NO:21 and 22, SEQ ID NO:23 and 24, SEQ ID NO:25 and 26, SEQ ID NO:27 and 28, SEQ ID NO:29 and 30, SEQ ID NO:31 and 32, SEQ ID NO:33~~ SEQ ID NOS: 33 and 34, or SEQ ID NO:35 SEQ ID NOS: 35 and 36, SEQ ID NO:37 and 38, SEQ ID NO:39 and 40, SEQ ID NO:41 and 42, SEQ ID NO:43 and 44, SEQ ID NO:45 and 46, SEQ ID NO:47 and 48, and SEQ ID NO:49 and 50.

22. (Original) The method of claim 10, wherein the nucleic acid-containing specimen comprises a tissue selected from the group consisting of brain, colon, urogenital, lung, renal, prostate, pancreas, liver, esophagus, stomach, hematopoietic, breast, thymus, testis, ovarian, and uterine.

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23. (Original) The method of claim 10, wherein the nucleic acid-containing specimen is selected from the group consisting of serum, urine, saliva, blood, cerebrospinal fluid, pleural fluid, ascites fluid, sputum, stool, and biopsy sample.

Claims 24-32 (Cancel)

33. (Currently amended) A method for detecting a ~~cellular proliferative disorder~~ associated with hypermethylation of CACNA1G colorectal adenoma or a cancer other than glioma, the method comprising contacting a nucleic acid-containing specimen from a subject with ~~an agent that provides a determination of the methylation state~~ SEQ ID NO:33 and SEQ ID NO:34 or with SEQ ID NO:35 and SEQ ID NO:36, wherein SEQ ID NO:33 and SEQ ID NO:34 are a primer pair for amplification of a first region of a CACNA1G CpG island, and wherein SEQ ID NO:35 and SEQ ID NO:36 are a primer pair for amplification of a second region of the CACNA1G CpG island comprising any of SEQ ID NO:35-42, wherein hypermethylation of one or both of the first region and the second region of the CACNA1G CpG island is indicative of the presence of the ~~cellular proliferative disorder~~ colorectal adenoma or the cancer other than glioma, thereby detecting the colorectal adenoma or the cancer other than glioma.

Claims 34-36. (Cancel)

37. (Currently amended) The method of claim 33, wherein the cancer is cellular ~~proliferative disorder~~ is colorectal cancer, colorectal adenoma, gastric cancer, lung cancer, breast cancer, hematopoietic tumors, prostate cancer, or acute myeloid leukemia (AML).

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38. (Currently amended) The method of claim 33, wherein the cancer is cellular ~~proliferative disorder is astrocytoma, glioblastoma,~~ medulloblastoma, lung cancer, renal cancer, endometrial cancer or neuroblastoma.

39. (New) The method of claim 33, wherein the cancer is colorectal cancer, gastric cancer, or acute myelogenous leukemia (AML).

40. (New) The method of claim 33, wherein the method further comprises contacting the nucleic acid-containing specimen from the subject with a primer pair for amplifying a fourth region of the CACNA1G CpG island wherein the primer pair is SEQ ID NO:39 and SEQ ID NO:40, a fifth region of the CACNA1G CpG island wherein the primer pair is SEQ ID NO:41 and SEQ ID NO:42, a sixth region of the CACANA1G CpG island wherein the primer pair is SEQ ID NO:43 and SEQ ID NO:44, a seventh region of the CACNA1G CpG island wherein the primer pair is SEQ ID NO:45 and SEQ ID NO:46, or an eighth region of the CACNA1G CpG island wherein the primer pair is SEQ ID NO:47 and SEQ ID NO:48, and wherein hypermethylation of one or more of the fourth region, the fifth region, the sixth region, the seventh region, or the eighth region of the CACNA1G CpG island is indicative of the presence of the cancer other than glioma or colorectal adenoma.

41. (New) A method for detecting colorectal adenoma, colorectal cancer, gastric cancer, or acute myelogenous leukemia (AML), comprising:

- a) contacting a nucleic acid-containing specimen from a subject with an agent that provides a determination of the methylation state of at least one of a fifth region, a sixth region, and a seventh region of a CpG island of a CACNA1G, wherein the fifth region is the region of the CACNA1G CpG island that is amplified by SEQ ID NO:41 and SEQ ID NO:42, wherein the sixth region is the region of the CACNA1G CpG island that is amplified by SEQ ID NO:42 and SEQ ID NO:43 and wherein the seventh region is the region of the CACNA1G CpG island that is amplified by SEQ ID NO:44 and SEQ ID NO:45, and
- b) detecting hypermethylation of at least one of the fifth region, the sixth region, and the seventh region, wherein hypermethylation of at least one of the fifth region, the sixth region, and the seventh region as compared to the same region of the CACNA1G gene in a subject not having colorectal adenoma, colorectal cancer, gastric cancer, or AML is indicative of the colorectal adenoma, colorectal cancer, gastric cancer, or AML.

42. (New) A method for detecting colorectal adenoma, colorectal cancer, gastric cancer, or acute myelogenous leukemia (AML), comprising contacting a nucleic acid-containing specimen from a subject with SEQ ID NO:41 and SEQ ID NO:42, with SEQ ID NO:43 and SEQ ID NO:44 or with SEQ ID NO:45 and SEQ ID NO:46, wherein SEQ ID NO:41 and SEQ ID NO:42 are a primer pair for amplification of a fifth region of a CACNA1G CpG island, wherein SEQ ID NO:43 and SEQ ID NO:44 are a primer pair for amplification of a sixth region of a CACNA1G CpG island, and wherein SEQ ID NO:45 and SEQ ID NO:46 are a primer pair for amplification of a seventh region of the CACNA1G CpG island, wherein hypermethylation of

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one or more of the fifth region, the sixth region, or the seventh region of the CACNA1G CpG island is indicative of the presence of the colorectal adenoma, colorectal cancer, gastric cancer, or the AML, thereby detecting the colorectal adenoma, colorectal cancer, gastric cancer, or the AML.